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Obesity and overweight are associated with worse survival in early-onset colorectal cancer

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ABSTRACT

Background: Obesity and its associated lifestyle are known risk factors for early-onset colorectal cancer and are associated with poor postoperative and survival outcomes in older patients. We aimed to investigate the impact of obesity on the outcomes of early-onset colorectal cancers.

Methods: Retrospective review of all patients undergoing primary resection of colon or rectal adenocarcinoma at our institution between 2015–2022. Patients who had palliative resections, resections performed at another institution, appendiceal tumors, and were underweight were excluded. The primary endpoint was survival according to the patient's body mass index: normal weight (18–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obesity (≥30 kg/m^2). Patient and tumor characteristics and survival were compared between the three groups.

Results: A total of 279 patients aged <50 years with colorectal cancer were treated at our hospital; 120 were excluded from the analysis for the following reasons: main treatment or primary resection performed at another hospital ($n = 97$), no resection/palliative resection ($n = 23$), or body mass index <18 kg/m^2 ($n = 2$). Of these, 157 patients were included in the analysis; 61 (38.9%) were overweight and 45 (28.7%) had obesity. Except for a higher frequency of hypertension in the overweight ($P = .062$) and obese ($P = .001$) groups, no differences in patient or tumor characteristics were observed. Mean overall survival was 89 months with normal weight, 92 months with overweight, and 65 months with obesity ($P = .032$). Mean cancer-specific survival was 95 months with normal weight, 94 months with overweight, and 68 months with obesity ($P = .018$). No statistically significant difference in disease-free survival (75 vs 70 vs 59 months, $P = .844$) was seen.

Conclusion: Individuals with early-onset colorectal cancer who are overweight or obese present with similar tumor characteristics and postoperative morbidity to patients with normal weight. However, obesity may have a detrimental impact on their survival. Addressing obesity as a modifiable risk factor might improve early-onset colorectal cancer prognosis.

Introduction

In 2020, colorectal cancer represented 9.4% of cancer-related deaths worldwide.[1] An increase in the incidence of early-onset colorectal cancer (EOCRC) affecting patients aged ≤50 years and its associated mortality has been reported for several decades.[1,2] The American Cancer Society recommended lowering the starting age of colorectal screening from 50 to 45 years.[3] This measure is expected to improve survival through diagnosis at an early stage and reduce cancer-related disabilities and costs.[4,5] Further measures are being taken to target preventable factors associated with EOCRC, particularly obesity and its associated lifestyle and sedentarism.[6,7] Almost half of the US population aged between 20 and 59 years has obesity.[8] In 2012, 21,800 colorectal cancer diagnoses were

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associated with an increased body mass index (BMI), 7,600 of which might have been prevented if the population's mean BMI had not increased over the last 30 years.[1] The risk of developing colorectal cancer among men is increasing by 9% with every 5 kg/m^2 increase in BMI.[7] The role of obesity in the development of EOCRC has already been described in addition to Western diet, microbiome alterations, smoking, sedentary lifestyle, and antibiotic use[2], although genetic and epigenetic alterations may also play an important role.[6] In addition to being a risk factor for colorectal cancer, an association between obesity and poor postoperative and oncologic outcomes has been previously described in the older population.[9-12]

Patients with EOCRC often have more aggressive tumor characteristics and more advanced tumor stage at diagnosis than older patients.[2,13] It is unclear whether patients with obesity who develop EOCRC have different tumor characteristics and survival rates compared with patients with ideal weight at the time of EOCRC diagnosis. Our study aimed to investigate the differences in tumor characteristics and postoperative and oncologic outcomes in a cohort of patients diagnosed with EOCRC stratified by their BMI category.

Methods

Patient selection and data analysis

After approval by our Institutional Review Board, all patients aged 18 to 50 years treated at our institution between 01/01/2015 and 12/31/2022 for colorectal adenocarcinoma were retrospectively reviewed. Only patients undergoing an oncologic resection of the primary tumor at our hospital were included in the final analysis. We excluded patients who underwent resection of their primary tumor at another institution, underwent palliative resection, did not have an oncologic resection (such as diversion ostomy only), had appendiceal cancers, and had a BMI <18kg/m^2 at the time of diagnosis. A medical record review of all patients who met the inclusion criteria was undertaken. Patients' characteristics, tumor stage, histopathologic characteristics, surgical outcomes, and follow-up (including disease recurrence and death) were reported in a designated REDCap database assigned specifically for this study by the authors. Patients were divided according to their BMI into normal weight (BMI: 18−24.9 kg/m^2), overweight (BMI: 25−29.9 kg/m^2), and obesity (BMI: ≥30 kg/m^2) groups. The Strengthening the Reporting of Observational Studies in Epidemiology checklist was used to report the methodology and findings.

Study endpoints

The primary endpoints were overall, cancer-specific, and disease-free survival stratified by the BMI category and tumor stage. The secondary outcomes were perioperative and short-term postoperative outcomes according to the BMI category.

Statistical analysis

Descriptive statistics were used. Continuous variables were expressed as a median and normal range and categorical variables as numbers and percentages. Comparisons between the groups

Table I
Patient characteristics of patients with early-onset colorectal cancer according to their body mass index

	Normal weight ($n = 51$)	Overweight ($n = 61$)	P^* value	Obesity ($n = 45$)	$P^\dagger$ value
Age at diagnosis	44 (40, 48)	44 (40, 47)	.640	45 (40, 48)	.176
Sex					
Female	24 (47.1)	25 (41.0)	.569	16 (35.6)	.351
Male	27 (52.9)	36 (59.0)		29 (64.4)	
Ethnicity					
White	26 (51.0)	36 (59.0)	.796	22 (48.9)	.684
Hispanic	11 (21.6)	12 (19.7)		12 (26.7)	
Black	8 (15.7)	8 (13.1)		5 (11.1)	
Asian/Pacific Islander	3 (5.9)	1 (1.6)		2 (4.4)	
Multi-racial	3 (5.9)	3 (4.9)		2 (4.4)	
Native American	0 (0.0)	1 (1.6)		2 (4.4)	
Comorbidity					
Hypertension	0 (0.0)	5 (8.2)	.062	11 (24.4)	.001
Hypercholesterolemia	2 (3.9)	9 (14.8)	.064	5 (11.1)	.338
COPD	0 (0.0)	0 (0.0)	NA	1 (2.2)	.95
Asthma	0 (0.0)	3 (4.9)	.249	2 (4.4)	.421
Renal insufficiency	0 (0.0)	1 (1.6)	1	2 (4.4)	.421
Diabetes mellitus	1 (2.0)	0 (0.0)	.455	2 (4.4)	.912
Inflammatory bowel disease	3 (5.9)	5 (8.2)	.726	2 (4.4)	1
History of bariatric surgery	0 (0.0)	0 (0.0)	NA	2 (4.4)	.421
Smoking					
Never	37 (72.5)	42 (68.9)	.616	34 (75.6)	.789
Former	10 (19.6)	16 (26.2)		9 (20.0)	
Active	4 (7.8)	3 (4.9)		2 (4.4)	
Alcohol					
Never	21 (41.2)	30 (50.8)	.339	18 (40.0)	1
Occasional	30 (58.8)	28 (47.5)		27 (60.0)	
Abusive	0 (0.0)	1 (1.7)		0 (0.0)	
CEA level at diagnosis	2.6 (1.4, 5)	2.5 (1.2, 6.9)	.847	2.8 (1.7, 9.7)	.157
Family history of colorectal cancer	14 (28.0)	19 (31.1)	.835	7 (15.6)	.226
First degree	10 (19.6)	13 (21.3)	1	4 (8.9)	.232
Genetic predisposition	3 (6.4)	7 (11.9)	.507	3 (6.7)	1

Data are represented as absolute number (percentage) or median (IQR).
CEA, carcinoembryonic antigen; *COPD*, chronic obstructive pulmonary disease; *NA*, not available.
* Comparison between patients with normal weight and overweight.
† Comparison between patients with normal weight and obesity.

Table II
Tumor characteristics of patients with early-onset colon cancer according to their body mass index

	Normal weight ($n = 24$)	Overweight ($n = 33$)	P^* value	Obesity ($n = 20$)	$P^\dagger$ value
Cancer localization					
Right colon	6 (25.0)	5 (15.2)	.551	4 (20.0)	.066
Transverse colon	3 (12.5)	2 (6.1)		0 (0.0)	
Left colon	1 (4.2)	3 (9.1)		6 (30.0)	
Sigmoid/Rectosigmoid junction	14 (58.3)	23 (69.7)		10 (50.0)	
Adenocarcinoma	20 (83.3)	32 (97.0)	.197	17 (85.0)	1
Mucinous carcinoma	3 (12.5)	1 (3.0)		3 (15.0)	
Signet ring cell carcinoma	1 (4.2)	0 (0.0)		0 (0.0)	
Grade					
G1 well differentiated	2 (8.3)	6 (18.2)	.580	4 (20.0)	.647
G2 moderately differentiated	14 (58.3)	19 (57.6)		11 (55.0)	
G3 poorly differentiated	5 (20.8)	7 (21.2)		4 (20.0)	
G4 undifferentiated	1 (4.2)	0 (0.0)		0 (0.0)	
Gx	2 (8.3)	1 (3.0)		1 (5.0)	
Tumor stage					
Stage I	2 (8.3)	7 (21.9)	.325	4 (21.1)	.633
Stage II	6 (25.0)	5 (15.6)		3 (15.8)	
Stage III	9 (37.5)	15 (46.9)		8 (42.1)	
Stage IV	7 (29.2)	5 (15.5)		4 (21.1)	
Lymphovascular invasion					
Absent	14 (58.3)	19 (57.6)	1	9 (45.0)	.545
Present	10 (41.7)	13 (39.4)		11 (55.0)	
Unknown	0 (0.0)	1 (3)		0 (0.0)	
Perineural invasion					
Absent	17 (70.8)	26 (78.8)	.620	15 (75.0)	1
Present	7 (29.2)	6 (18.2)		5 (25.0)	
Unknown	0 (0.0)	1 (3.0)		0 (0.0)	
Tumor deposit					
No deposit	9 (37.5)	15 (45.5)	.649	9 (45.0)	.678
One deposit	1 (4.2)	0 (0.0)		0 (0.0)	
More than one deposit	3 (12.5)	5 (15.2)		5 (25.0)	
Unknown	11 (45.8)	13 (39.3)		6 (30.0)	
Neoadjuvant chemotherapy	4 (16.7)	6 (18.2)	1	3 (15.0)	1
AJCC/CAP tumor regression grade					
Complete response	0 (0.0)	1 (16.7)	1	0 (0.0)	1
Moderate response	0 (0.0)	0 (0.0)		0 (0.0)	
Minimal response	2 (50.0)	2 (33.3)		1 (33.3)	
Poor response	0 (0.0)	0 (0.0)		1 (33.3)	
Unknown	2 (50.0)	3 (50.0)		1 (33.3)	
Resection completeness					
R0	22 (91.7)	31 (93.9)	.751	19 (95.0)	1
R1	2 (8.3)	1 (3.0)		1 (5.0)	
R2	0 (0.0)	0 (0.0)		0 (0.0)	
Rx	0 (0.0)	1 (3.0)		0 (0.0)	
Microsatellite instability	4 (18.2)	5 (17.2)	1	2 (11.8)	.679
Microsatellite stable	18 (81.8)	24 (82.8)		15 (88.2)	
RAS mutation	5 (35.7)	10 (45.5)	.732	8 (66.7)	.238
RAS wildtype	9 (64.3)	12 (54.5)		4 (33.3)	
NRAS mutation	0 (0.0)	1 (5.0)	1	0 (0.0)	1
NRAS wildtype	13 (100.0)	19 (95.0)		11 (100.0)	
BRAF mutation	0 (0.0)	0 (0.0)	NA	0 (0.0)	NA
BRAF wildtype	14 (100.0)	22 (100.0)		11 (100.0)	
Adjuvant chemotherapy	16 (66.7)	21 (63.6)	1	12 (60.0)	.757

Data are represented as absolute number (percentage) or median (IQR).
AJCC/CAP, American Joint Committee on Cancer/College of American Pathologists; *NA*, not available.
* Comparison between patients with normal weight and overweight.
† Comparison between patients with normal weight and obesity.

were performed using the Fisher exact test and Chi-square analysis for categorical variables, and Mann–Whitney *U* test and Student's *t* test for continuous variables, as appropriate. Disease-free survival was defined as the time from the primary tumor resection to the date of recurrence or last follow-up. Patients with tumor progression were defined as patients who were not disease-free after resection of the primary tumor (macroscopic incomplete resection or non-resected metastasis) and were excluded from this analysis. Overall and cancer-specific survival was defined as the time from the primary tumor resection to the date of death or last follow-up. Cancer-specific survival reported only deaths related to colorectal cancer. Death for other or unknown reasons was excluded from the cancer-specific analysis. Survival analyses were conducted using the Kaplan–Meier statistics and log-rank test. Statistical analyses were done using EZR (version 1.61, Jichi Medical University Saitama Medical Center) and R software (version 4.3.1, R Foundation for Statistical Computing).

Results

Patient selection

From 2015 to 2022, 279 patients with early-onset colorectal cancer were treated at our hospital. Patient selection is summarized in the flowchart in Supplementary Figure S1. Patients who had their main treatment or primary resection performed at another hospital

Table III
Tumor characteristics of patients with early-onset rectal cancer according to their body mass index

	Normal weight ($n = 27$)	Overweight ($n = 28$)	P^* value	Obesity ($n = 25$)	$P^\dagger$ value
Cancer localization					
Distal rectum	9 (33.3)	14 (51.9)	.419	12 (48.0)	.642
Middle rectum	10 (37.0)	8 (29.6)		7 (28.0)	
Proximal rectum	8 (29.6)	5 (18.5)		6 (24.0)	
Adenocarcinoma	25 (92.6)	27 (96.4)	.361	25 (100.0)	.491
Mucinous carcinoma	2 (7.4)	0 (0.0)		0 (0.0)	
Signet ring cell carcinoma	0 (0.0)	1 (3.6)		0 (0.0)	
Grade					
G1 well differentiated	3 (11.5)	2 (7.1)	.804	3 (12.0)	.345
G2 moderately differentiated	20 (76.9)	24 (85.7)		14 (56.0)	
G3 poorly differentiated	2 (7.7)	2 (7.1)		4 (16.0)	
G4 undifferentiated	0 (0.0)	0 (0.0)		0 (0.0)	
Gx	1 (3.8)	0 (0.0)		4 (16.0)	
Tumor stage					
Stage I	3 (11.1)	3 (11.1)	.966	4 (16.0)	.971
Stage II	5 (18.5)	3 (11.1)		4 (16.0)	
Stage III	16 (59.3)	18 (66.7)		14 (56.0)	
Stage IV	3 (11.1)	3 (11.1)		3 (12.0)	
Lymphovascular invasion					
Absent	21 (77.8)	18 (64.3)	.375	16 (64.0)	.436
Present	6 (22.2)	10 (35.7)		8 (32.0)	
Unknown	0 (0.0)	0 (0.0)		1 (4.0)	
Perineural invasion					
Absent	24 (88.9)	25 (89.3)	1	19 (76.0)	.346
Present	3 (11.1)	3 (10.7)		5 (20.0)	
Unknown	0 (0.0)	0 (0.0)		1 (4.0)	
Tumor deposit					
No deposit	15 (55.5	12 (42.9)	.468	11 (44.0)	.153
One deposit	2 (7.4)	1 (3.6)		0 (0.0)	
More than one deposit	2 (7.4)	5 (17.9)		5 (20.0)	
Unknown	8 (29.6)	10 (35.7)		9 (36.0)	
Neoadjuvant chemoradiation	17 (63.0)	24 (85.7)	.068	21 (84.0)	.121
Clinical treatment response					
Near/complete response	2 (11.8)	9 (37.5)	.071	8 (38.1)	.09
Partial response	7 (41.2)	5 (20.8)		5 (23.8)	
Unchanged	1 (5.9)	0 (0.0)		0 (0.0)	
Progression	0 (0.0)	1 (4.2)		1 (4.8)	
Unknown	7 (41.2)	9 (37.5)		7 (33.3)	
AJCC/CAP tumor regression grade					
Complete response	3 (16.7)	4 (16.7)	.636	9 (42.9)	.262
Moderate response	3 (16.7)	7 (29.2)		1 (4.8)	
Minimal response	8 (44.4)	6 (25.0)		7 (33.3)	
Poor response	3 (16.7)	3 (12.5)		2 (9.5)	
Unknown	1 (5.6)	4 (16.7)		2 (9.5)	
Resection completeness					
R0	26 (96.3)	26 (92.9)	1	22 (88.0)	.341
R1	1 (3.7)	2 (7.1)		3 (12.0)	
R2	0 (0.0)	0 (0.0)		0 (0.0)	
Rx	0 (0.0)	0 (0.0)		0 (0.0)	
Circumferential margin					
>1 mm	25 (96.2)	25 (92.6)	1	22 (88.0)	.35
≤1 mm	1 (3.8)	2 (7.4)		3 (12.0)	
Intactness of mesorectum					
Complete	18 (69.2)	15 (55.6)	.404	16 (64.0)	.953
Nearly complete	2 (7.7)	5 (18.5)		3 (12.0)	
Incomplete	5 (19.2)	7 (25.9)		5 (20.0)	
Unknown	1 (3.8)	0 (0.0)		1 (4.0)	
Microsatellite instability	2 (9.5)	2 (7.4)	1	0 (0.0)	.49
Microsatellite stable	19 (90.5)	25 (92.6)		18 (100.0)	
RAS mutation	6 (42.9)	8 (38.1)	1	4 (26.7)	.45
RAS wildtype	8 (57.1)	13 (61.9)		11 (73.3)	
NRAS mutation	0 (0.0)	0 (0.0)	1	1 (7.1)	1
NRAS wildtype	14 (100.0)	18 (100.0)		13 (92.9)	
BRAF mutation	0 (0.0)	0 (0.0)	NA	0 (0.0)	NA
BRAF wildtype	14 (100.0)	18 (100.0)		14 (100.0)	
Adjuvant chemotherapy	15 (55.6)	22 (78.6)	.089	11 (44.0)	.579

Data are represented as absolute number (percentage) or median (IQR).
AJCC/CAP, American Joint Committee on Cancer/College of American Pathologists; *NA*, not available.
* Comparison between patients with normal weight and overweight.
† Comparison between patients with normal weight and obesity.

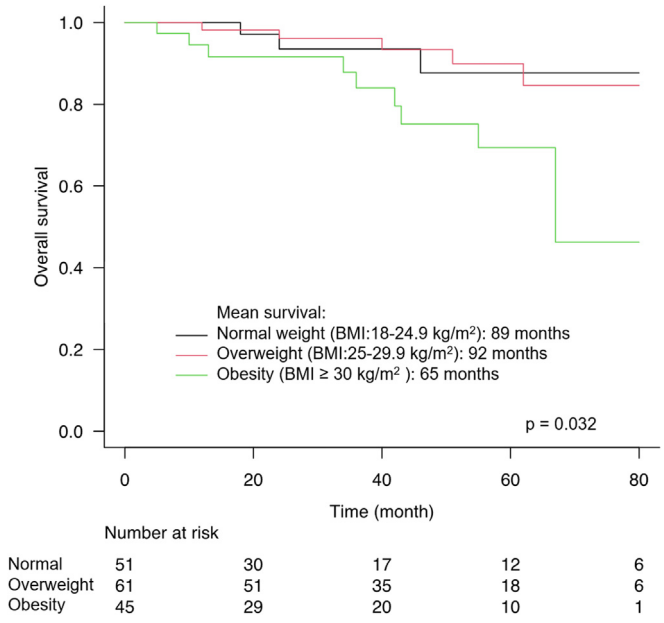

Figure 1. Overall survival of patients with early-onset colorectal cancer according to their body mass index.

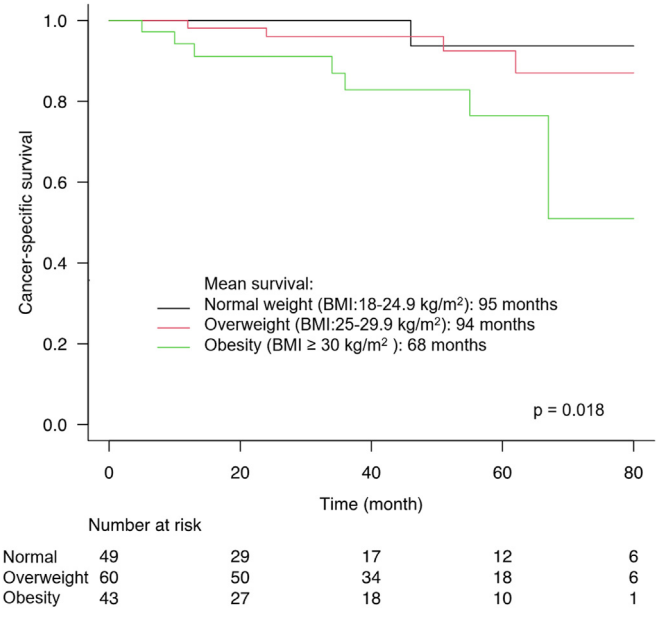

Figure 2. Cancer-specific survival of patients with early-onset colorectal cancer according to their body mass index.

(n = 97) and those without resection of their primary tumor or palliative resection were excluded (n = 23). Two patients with a BMI <18 kg/m^2 were excluded from the analysis. In total, 157 patients were included. Overall, 62 (39.5%) patients were overweight and 45 (28.7%) had obesity. The median follow-up was 37 months (IQR 18, 60).

Patient and tumor characteristics

The cohort's median age was 44 (range 26–50) years, and 92 (58.6%) patients were male. All patients' characteristics are summarized in Table I. Except for a higher frequency of hypertension in the overweight (P = .062) and obese (P = .001) groups, no differences in patients' characteristics were observed. Tumor characteristics, stage, and resection quality are presented in Table II for colon cancer (n = 77) and Table III for rectal cancer (n = 80).

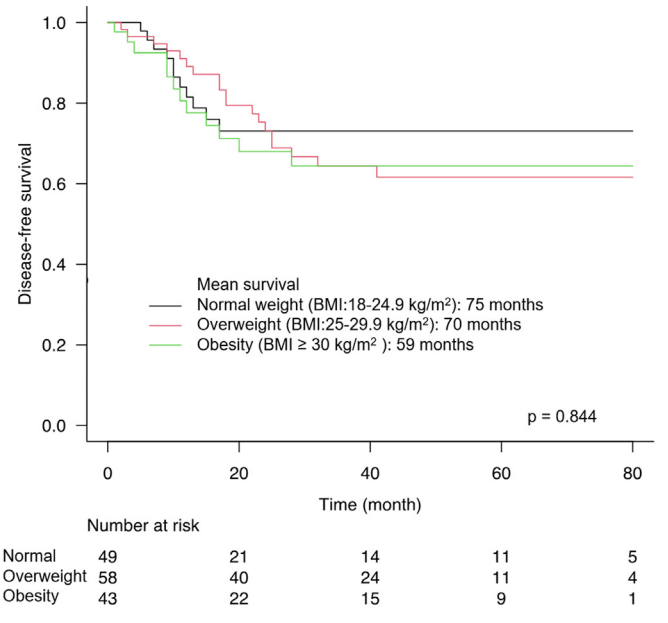

Figure 3. Disease-free survival of patients with early-onset colorectal cancer according to their body mass index.

Overall cancer-specific and disease-free survival

Patients with obesity had worse overall and cancer-specific survival than those in the ideal weight range (Figures 1 and 2). The mean overall survival of patients with normal weight compared with patients who were overweight and obese was 89 versus 92 versus 65 months (P = .032), and the mean cancer-specific survival was 95 versus 94 versus 68 months (P = .018). There was no statistically significant difference in disease-free survival (75 vs 70 vs 59 months, P = .844) (Figure 3). Stage-stratified cancer-specific and disease-free survival is shown in Supplementary Figures S2–S4). In a Cox regression analysis adjusted for age, sex, tumor stage IV, cancer localization (rectum versus colon), adjuvant and neoadjuvant treatment, and resection completeness obesity was associated with worse cancer-specific survival (hazard ratio [HR] (95% CI): 11.56 [1.21, 110], P = .034) but not overweight (HR [95% CI] 3.16 [0.31, 32.59], P = .33); obesity and overweight were not associated with worse overall survival (obesity: HR [95% CI] 3.56 (0.83, 15.24, P = .087, overweight: HR (95% CI) 1.32 (0.26, 6.54, P = .74).

Perioperative outcomes

Perioperative outcomes are presented in Table IV. Patients with normal weight and those who were overweight presented more often with tumor obstruction or perforation (normal weight: 11.8%, versus obesity: 0% P = .051). Obese patients more often underwent combined transanal and laparoscopic surgery compared with patients with normal weight (P = .015). Patients with obesity had a longer operative time (240 vs 300 minutes, P = .014). Postoperative morbidity did not differ between the three groups, and there was no postoperative mortality. Four patients refused adjuvant chemotherapy, and in four additional patients this information was

Table IV
Surgery characteristics of patients with early-onset colorectal cancer according to their body mass index

	Normal weight ($n = 51$)	Overweight ($n = 61$)	P^* value	Obesity ($n = 45$)	$P^\dagger$ value
Right hemicolectomy	6 (11.8)	4 (6.6)	.752	3 (6.7)	.631
Left hemicolectomy	9 (17.6)	15 (24.6)		13 (28.9)	
Subtotal colectomy	3 (5.9)	3 (4.9)		1 (2.2)	
Anterior resection	25 (49.0)	31 (50.8)		23 (51.1)	
Abdominoperineal amputation	6 (11.8)	4 (6.6)		3 (6.7)	
Total proctocolectomy	2 (3.9)	4 (6.6)		2 (4.4)	
Cancer diagnosis at surgery					
Establish	47 (92.2)	58 (95.1)	.402	45 (100.0)	.159
Suspected	2 (3.9)	3 (4.9)		0 (0.0)	
Unknown	2 (3.9)	0 (0.0)		0 (0.0)	
Finding at surgery					
Obstruction	3 (5.9)	5 (8.2)	.790	0 (0.0)	.051
Perforation	2 (3.9)	1 (1.6)		0 (0.0)	
Other	1 (2.0)	2 (3.3)		0 (0.0)	
Anastomosis performed during resection	42 (82.4)	52 (85.2)	.798	41 (91.1)	.341
Stoma					
No stoma	24 (47.1)	24 (39.3)	.655	18 (40.0)	.332
Prior surgery	0 (0.0)	2 (3.3)		0 (0.0)	
Protective loop ileostomy	19 (37.3)	26 (42.6)		23 (51.1)	
End Ileo-/colostomy	8 (15.7)	9 (14.8)		4 (8.9)	
Access					
Laparoscopic	34 (66.7)	29 (47.5)	.166	18 (40.0)	.015
Laparoscopic and transanal	5 (9.8)	13 (21.3)		15 (33.3)	
Open	10 (19.6)	17 (27.9)		8 (17.8)	
Robotic	2 (3.9)	2 (3.3)		4 (8.9)	
Conversion to open	2 (3.9)	3 (4.9)	1	3 (6.7)	.886
Operation length (min)	240 (159, 319)	248 (170, 345)	.498	300 (209, 370)	.014
Length of stay (d)	4 (3, 7)	6 (4, 80)	.046	5 (4, 8)	.104
Postoperative complication at 30 d	15 (29.4)	23 (37.7)	.425	13 (28.9)	1
Major postoperative complication at 30 d	4 (7.8)	4 (6.6)	1	1 (2.2)	.437
Postoperative ileus	5 (9.8)	8 (13.1)	.769	5 (11.1)	1
Anastomotic leak	3 (5.9)	1 (1.6)	.329	0 (0.0)	.287
Postoperative bleeding	1 (2.0)	0 (0.0)	.455	2 (4.4)	.912
SSI superficial	0 (0.0)	4 (6.6)	.124	1 (2.2)	.95
SSI deep	0 (0.0)	1 (1.6)	1	1 (2.2)	.95
SSI organ/space	3 (5.9)	6 (9.8)	.506	5 (11.1)	.579
Reintervention					
Endoscopic	0 (0.0)	0 (0.0)	NA	45 (100.0)	NA
Radiological	2 (3.9)	2 (3.3)	1	5 (11.1)	.338
Laparoscopic	2 (3.9)	0 (0.0)	.205	0 (0.0)	.531
Open surgery	3 (5.9)	2 (3.3)	.658	1 (2.2)	.701
Readmission at 30 d	7 (13.7)	8 (13.1)	1	2 (4.4)	.228
Postoperative mortality at 30 d	0 (0.0)	0 (0.0)	NA	0 (0.0)	NA
Follow-up (mo)	24 (14, 56)	44 (28, 62)	.01	36 (11, 58)	.921

Data are represented as absolute number (percentage) or median (IQR).
SSI, surgical site infection; *NA*, not available.
* Comparison between patients with normal weight and overweight.
† Comparison between patients with normal weight and obesity.

not available. The remaining patients were treated according to the current guidelines, with 98 (62.4%) patients undergoing adjuvant chemotherapy.

Discussion

The present study found that patients with EOCRC had similar disease stages and tumor characteristics regardless of their BMI category. However, obese patients had worse overall and cancer-specific survival than those with a normal BMI.

Obesity is a well-known risk factor for colorectal cancer, causing chronic systemic inflammation, increased insulin-dependent growth factor due to insulin resistance, and intestinal dysbiosis.[6,14] At diagnosis, 66% of patients were overweight or obese, consistent with the current rates observed in the US population.[1] However, we observed more overweight (38.3%) than obese patients (27.7%), which may be explained by the weight loss occurring before the diagnosis of EOCRC. The association between colorectal cancer and obesity is often underestimated due to weight loss typically accompanying the oncologic burden.[15]

Hypertension was present in only one-quarter and one-tenth of patients who were obese or overweight, respectively. Except for hypertension, overweight or individuals with obesity had similar characteristics to patients with normal weight. The majority of patients can, therefore, be defined as having "metabolically healthy obesity." Interestingly, the incidence of diabetes was also low (<4.4%), even though obesity and type 2 diabetes have been associated with an increased risk of colorectal cancer.[14] Obesity might promote cancer at an early stage in metabolically healthy patients. An unhealthy lifestyle, sedentarism, and intestinal microbiome alteration are often associated with obesity and probably have a direct influence on cancer development.[2,6,16] Although not significant, patients with normal weight and those who were overweight more often had a positive family history of colorectal cancer than patients with obesity (28%, 30.6%, and 15.6%, respectively).

In addition to the increased risk of cancer, individuals with obesity are more vulnerable, as obesity is associated with a lower socioeconomic status, poor access to health care, an increased risk of not undergoing a screening colonoscopy, and not receiving chemotherapy doses adapted to their weight.[9,12,16,17] Concern has

been raised that the reduction of the age for screening colonoscopy might not reach patients with obesity. Previous studies reported more advanced cancer in patients with obesity.[9,11] In our study, the tumor stage was not different in individuals who were overweight and obese when compared with normal weight. This might be the result of efforts undertaken to improve screening in this specific population.

Postoperative outcomes were similar in patients regardless of their weight category. The EuroSurg Collaborative reported that, in a multicentric cohort of 2519 patients undergoing gastrointestinal surgery, obesity was not associated with major complications.[18] Conversely, their meta-analysis highlighted a higher risk of complications in patients with obesity undergoing gastrointestinal surgery for malignancy. These results were also supported by the STARSurg Collaborative cohort.[19] The effect of obesity on surgical outcomes is complex and multifaceted, where factors such as BMI severity, duration, associated comorbidities, and the localization of the tumor might nuance the relationship between obesity and surgical outcome. Looking at the technical challenge that obesity represents, minimally invasive surgery and options such as combined transanal access might be especially beneficial in patients with obesity. Although operative times were longer, the patients seemed to benefit from this approach when evaluating postoperative outcomes.

Even with similar tumor stages and postoperative outcomes, our results highlighted an association between obesity and poor survival in patients with EOCRC. This association has been previously described in older patients.[9,11,12,20] One explanation could be the paradox of sarcopenic obesity. Cancer-related weight loss does not only entail a loss of fat tissue but also skeletal muscle loss.[21] Chronic systemic inflammation in patients with colorectal cancer may increase weight loss, leading to sarcopenia, metabolic dysfunction, and a negative impact on the oncologic outcomes.[22,23] Sarcopenic obesity is associated with higher overall cancer-related mortality and higher postoperative morbidity.[24-26] Data on the prevalence and impact of sarcopenic obesity on young patients with cancer are lacking.

Study limitations

Our study has several limitations. As a retrospective review in a single center, including a relatively small sample, the results should be cautiously interpreted. Even if tumor stage and characteristics were well balanced between individuals with normal weight, overweight, and obesity, minor heterogeneity in the surgical technique and team, cancer subtype, and treatment might have had an impact on our results. However, studies specifically evaluating EOCRC and its relation to obesity are limited, even though the numbers of EOCRC and obesity continue to increase each year. The authors think the present data are useful to raise awareness of obesity and its impact on cancer survival and to promote obesity prevention and treatment as a part of strategies for EOCRC prevention and outcomes improvement. Further studies on the subject should be encouraged to better understand the relationship between obesity and cancer development.

In conclusion, obesity may be associated with worse survival and treatment outcomes among affected individuals. In addition to primary prevention, addressing obesity as a modifiable risk factor may also have positive implications for EOCRC prognosis.

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Conflict of interest/Disclosure

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [https://10.1016/j.surg.2024.03.037].

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